



# VA Research Currents

Update from the Office of Research and Development...

## At the one-year mark, we need your feedback

By John R. Feussner, MD, MPH, *Chief R&D Officer*

**T**his issue marks one year of publication for *VA Research Currents*. It seems appropriate at this point to ask for your feedback. We want this newsletter to be a useful tool that will help you keep abreast of the achievements of your VA colleagues and stay connected to our nationwide research community.

In the past twelve monthly issues, we've reported on important findings by VA investigators in all areas of our research enterprise—from basic medical science, such as the article to the right on wasting syndrome, to rehabilitation, clinical trials and health services research. Among the topics we

wrote about: how VA compares to the private sector for heart attack care; the use of opiates for chronic pain; probing the relationship between homocysteine and cardiovascular disease; VA's role in developing artificial retinas; and rapid blood tests that help emergency-room physicians diagnose heart attack

You also read coverage of special events, such as a VA-National Institutes of Health roundtable on prosthetics, our national Research Week celebrations, and the opening of new centers of excellence. You read messages from the directors of the four research services about critical issues

see **FEEDBACK** on pg. 3

## Study: Physicians not stressing flu vaccine enough

Researchers at the Minneapolis VA Medical Center determined that health care providers are not making the most of their opportunities to give influenza and pneumococcal vaccinations to elderly and high-risk patients. In an article in the Dec. 10 *Archives of Internal Medicine*, lead author Kristin Nichol, MD, asserts that doctors may be missing many opportunities to provide vaccinations, with a significant number of doctors surveyed indicating that they do not strongly recommend shots to these patients.

Of 1,874 doctors responding to a survey, about one in seven generalists,

and one in four sub-specialists, failed to "very strongly recommend" flu shots to their elderly patients. The physicians were selected from the American Medical Association master list.

Since more than 60 percent of all elderly persons receive their flu shots at the doctor's office, physicians play a critical role in immunizing the elderly. According to Dr. Nichol, it is important that doctors make the most of the immunization opportunities that occur every day.

"There are very simple and effective

see **VACCINATION** on pg. 4

## VA scientists find key to 'wasting syndrome'

VA researchers and colleagues discovered a biochemical mechanism that may explain wasting syndrome, a condition that causes severe weight loss and weakness in patients with chronic inflammatory diseases and often hastens their death. The findings appeared in the Dec. 3 *EMBO* (European Molecular Biology Organization) *Journal*.

A team led by Martina Buck, PhD, and Mario Chojkier, MD, of the VA San Diego Healthcare System pinpointed the biological chain of events that caused wasting in mice, then identified the same process in liver tissue from cancer patients. They said the striking similarity between the condition in mice and humans will expedite the development of new treatments that may help patient with cancer, AIDS and other serious degenerative diseases.

"When we saw that it was virtually identical in animals and humans, we were ecstatic," said Dr. Chojkier, senior author on the study. "What we've described in animals has much greater relevance than we ever thought to human wasting syndrome. We're optimistic this will bring hope and relief very quickly to the bedside."

The investigators described the steps by which tumor necrosis factor (TNF) alpha, an immune-system protein, prevents the production of albumin. Low levels of albumin, a critical

see **WASTING** on pg. 3

## Recent publications and presentations

Below is a sampling of recent publications and presentations by VA investigators. Due to space constraints, only VA authors and affiliations are noted. Send notification of upcoming publications and presentations to R&D Communications by e-mail at [researchinfo@vard.org](mailto:researchinfo@vard.org); or by fax at (410) 962-0084. Include the manuscript title, journal title and publication date (if known), abstract, and full names and degrees of all VA-affiliated authors or presenters. If you feel the publication may be newsworthy for the general public, please indicate so.

"Barriers to the Use of Electronic Adherence Monitoring in an HIV Clinic." Christopher S. Wendel, MS; M. Jane Mohler, PhD; Kendall Kroesen, PhD; Neil M. Ampel, MD; Allen L. Gifford, MD. **Tucson and San Diego (ALG).** *Annals of Pharmacotherapy*, Sept. 2001.

"Comparing Methods to Identify General Internal Medicine Clinic Patients with Chronic Heart Failure." Edmund M. Udris, MPH; David H. Au, MD, MS; Mary B. McDonell, MS; Donald C. Martin, PhD; William M. Tierney, MD; Stephan D. Fihn, MD, MPH. **Seattle and Indianapolis (WMT).** *American Heart Journal*, Dec. 2001.

### VA Research Currents

is published monthly for the  
Office of Research and Development  
of the Dept. of Veterans Affairs  
by VA R&D Communications  
103 S. Gay St., Rm. 517  
Baltimore, MD 21202  
(410) 962-1800, ext. 223  
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"Direction of Action is Represented in the Ventral Premotor Cortex." Donna S. Hoffman, PhD; Peter L. Strick, PhD. **Pittsburgh.** *Nature Neuroscience*, Oct. 2001.

"Does Social Support Buffer Functional Decline in Elderly Patients with Unipolar Depression? Hayden B. Bosworth, PhD. **Durham.** *American Journal of Psychiatry*, Nov. 2001.

"Impact of Comorbidity on Predicted Hospital Mortality in ICU Patients." Joseph Johnston, MD. **Cincinnati.** Annual meeting of the Society for Medical Decision-Making, Oct. 2001.

"Mobility in Multiple Sclerosis." Michael L. Boninger, MD. **Pittsburgh.** *Multiple Sclerosis Quarterly Report*, fall 2001.

"Predicting Postoperative Pulmonary Complications: The Sleeping Giant Stirs." Valerie A. Lawrence, MD. **San Antonio.** *Annals of Internal Medicine*, Nov. 20, 2001.

"Retrospective Evaluation of the Effect of Valproate Therapy on Transaminase Elevations in Patients with Hepatitis C." Rex S. Lott, PharmD; Karl J. Madaras-Kelly, PharmD. **Boise.** *Pharmacotherapy*, Nov. 2001.

"A Spontaneously Arising Mutation in Connexin 32 with Repeated Passage of FRTL-5 Cells Coincides with Increased Growth Rate and Reduced Thyroxine Release." Lora M. Green, PhD. **Loma Linda.** *Journal of Molecular Endocrinology*, Oct. 2001.

"Treating the Cognitively Impaired Older Adult with Cognitive-Behavioral Therapy." A. Lynn Snow, PhD; David Powers, PhD; L. Siskin, PhD; S. Ogland-Hand, PhD. **Houston.** Annual meeting of the Gerontological Society of America, Nov. 2001.

"Underuse of Primary *Mycobacterium Avium* Complex and

*Pneumocystis Carinii* Prophylaxis in the United States." Steven M. Asch, MD, MPH; Allen L. Gifford, MD; Samuel Bozzette, MD, PhD. **Los Angeles and San Diego (ALG).** *Journal of Acquired Immune Deficiency Syndrome*, Dec. 2001.

"Validation of a Specific Activity Questionnaire to Estimate Exercise Tolerance in Patients Referred for Exercise Testing." Jonathan Myers, PhD; Victor Froelicher, MD. **Palo Alto.** *American Heart Journal*, Dec. 2001.

"Variations on the CAGE Alcohol Screening Questionnaire: Strengths and Limitations in VA General Medical Patients." Katherine A. Bradley, MD, MPH; Daniel R. Kivlahan, PhD; Kristen R. Bush, MPH; Mary B. McDonell, MS; Stephan D. Fihn, MD, MPH. **Seattle.** *Alcoholism: Clinical and Experimental Research*, Oct. 2001.

## Presentations from national meeting on Web

Presentations from the recent national meeting of VA Research and Development, held Oct. 29 – 31 in Keystone, Colo., are available in Powerpoint and HTML formats on the VA R&D website at [www.va.gov/resdev/fr/frmtngs/2001annual/post\\_presentations.cfm](http://www.va.gov/resdev/fr/frmtngs/2001annual/post_presentations.cfm).

Among the topics covered: the safety of research staff; the use of animals in research; VERA budgets; the protection of human subjects; tissue and genetic information banks; conflicts of interest; technology transfer; information technology; VA nonprofit research and education corporations; and the results of VA investigator satisfaction surveys. There are also updates from chief R&D officer Dr. John R. Feussner and the directors of the four research services.

## Wall St. Journal feature on VA quality improvement cites role of research

**A**ccording to a Dec. 10 *Wall Street Journal* article, “VA is leading a nascent movement to unlock the data lurking in hospitals to help doctors improve patient care and reduce errors.” The page-one feature chronicled VA’s recent quality improvement efforts and cited as a critical element the partnership between clinicians and researchers.

“A new patient safety center is training doctors and others to analyze errors and avoid repeating them,” said the article. “The VHA is bringing researchers and physicians together to discuss the latest medical literature and identify the best treatments for various diseases. ... The VHA isn’t alone in

these efforts, but it is doing so on a unique scale, leveraging its big budget and 1,300 hospitals and outpatient clinics in a way that no other health-care system can.”

The article describes VA’s Quality Enhancement Research Initiative (QUERI) as “a drive to systematically translate research findings into better health-care practices,” and cites the example of how a VA study of in-home monitoring for patients on anti-clotting medication may reduce the need for hospital or clinic visits.

The article details other ways in which VA has been successful in getting the “health-care and research sides to talk to each other,” and cites

the leadership in this area of chief R&D officer John R. Feussner, MD, MPH.

The article closes with a quote from Jonathan B. Perlin, director of VA’s Office of Quality and Performance, on the effectiveness of VA health-services researchers in measuring and improving clinicians’ adherence to practice guidelines. For example, the rate of vaccination for pneumonia at VA hospitals is now about 84 percent, compared to a national average of only 50 percent.

“Measurement ... changes behavior,” said Dr. Perlin. “Physicians don’t want to be laggards.”

### WASTING (cont. from pg. 1)

protein made in the liver, are a keynote of wasting.

TNF-alpha and low albumin had for years been implicated in wasting, but the connection between the two was a mystery. Drs. Buck and Chojkier showed that TNF alpha causes oxidative stress in the liver cell and boosts the production of the free-radical gas nitric oxide. It also causes the addition of a phosphorous molecule to a protein called C/EBP beta, which normally joins DNA in the nucleus of the cell to make other proteins, such as albumin. Central to the researchers’ finding was that this extra phosphorous causes the C/EBP beta to shuttle out of the nucleus into the cytoplasm, where transcription from the albumin gene can no longer take place and the protein is not produced.

The researchers found several ways of stopping the downward spiral caused by TNF- alpha. One way was to treat TNF-alpha-enhanced mice with vitamin E and other antioxidants. This blocked the chain of events leading to the “nuclear export” of C/EBP beta. According to Dr. Chojkier, antioxidants such as vitamin E might halt wasting in humans if these supplements were delivered in very high amounts—or even better, if they were targeted to the liver.

“One solution will be to find a liver-specific antioxidant,” he said. “With the technology we have today, this is very feasible. We believe this will provide an exciting avenue for intervention.”

Catabolic wasting, or cachexia, affects about half of all patients with cancer and AIDS and also affects patients with bacterial and parasitic diseases, rheumatoid arthritis, and chronic diseases of the bowel, liver, lungs and heart. Infusions of albumin are occasionally used to treat the condition, but the treatment is expensive, complicated, and only suitable for certain patients. ■

### FEEDBACK (cont. from pg. 1)

and timely initiatives. You learned of new funding opportunities, upcoming meetings and courses, and prestigious awards earned by your fellow VA scientists.

At this point, we’d like to hear what you would like to see in the newsletter: More extensive reporting on major findings? More listings of publications and presentations by VA investigators? Additional funding opportunities? Given the other publications you read in your busy day, how do you think *VA Research Currents* can best fulfill its mission to provide “news for the VA research community”?

Please take a few minutes to send an e-mail to the editor of this newsletter, at [researchinfo@vard.org](mailto:researchinfo@vard.org), to share your thoughts. In the coming year, we will make every effort to incorporate your ideas, along with those of your colleagues, to make this a publication you look forward to reading, and one that helps you in the vital work you do for VA and our nation’s veterans. ■

## Career milestones

### Award for St. Louis Alzheimer's researcher

John E. Morley, MD, director of the Geriatric Research, Education and Clinical Center at the St. Louis VA Medical Center, received the 2001 Gayle A. Olson and Richard D. Olson Prize from the University of New Orleans and the journal *Peptides* for his article titled "Alzheimer's Disease through the Eye of a Mouse," about the behavioral effects of peptides on learning and memory. Dr. Morley received a cash prize of \$2,500 and a trip to the university to deliver the keynote address at this year's Olson Prize Seminar.

### Miami ACOS honored at retirement

Friends and colleagues from VA and the University of Miami gathered Nov. 17 to salute Lawrence M. Fishman, MD, FACP, upon his retirement from

VA. Dr. Fishman served since 1975 as associate chief of staff for research and development at the Miami VA Medical Center.

Mindy Aisen, MD, Director of the Rehabilitation Research and Development Service, presented Dr. Fishman with a commendation from the Office of Research and Development. She and other speakers lauded him for his achievements as a teacher, physician, scientist and research administrator.

"I am very proud to be a member of the 'Fishman family,'" added Gustavo Godoy, administrative officer for research at the Miami VAMC. "I hope to carry on the Fishman mission, which has always been the pursuit of research excellence."

Amid praise for his accomplishments over 26 years, Dr. Fishman quipped modestly that the testimonial dinner felt like an "an out-of-body experience." He said above all he treasures the friendships and professional associations he developed in his VA service, noting that "special people are the most important reward one can have."

### VACCINATION (cont. from pg. 1)

strategies that doctors can use to increase their patient vaccination rates—some as simple as reminding the patient with a post card or telephone call before flu season begins," said Dr. Nichol. "Doctors can be reminded to make the most of their immunization opportunities by simple flagging the charts of patients who have not received a shot. Standing orders for nurses to offer and administer vaccinations to eligible patients are also highly effective."

According to the article, influenza and pneumococcal diseases cause tens of thousands of deaths every year. Of all vaccine-preventable diseases, these two are the most deadly. More than 90 percent of those killed are the elderly and others with high-risk medical conditions.

"We hope this VA study will encourage generalists and sub-specialists to take ownership of this immunization issue among their elderly and high risk patients," said Dr. Nichol. "However, we strongly recommend that patients take it upon themselves to bring up the subject of vaccination as well." ■

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